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Master's Thesis

Design of highly efficient organic photocatalysts for
visible-light driven reductive dehalogenation of aryl
halides

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Department of Materials Science and Engineering

Graduate School of UNIST

2019

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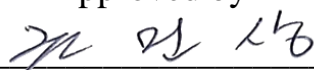
Design of highly efficient organic photocatalysts for visible-light driven reductive dehalogenation of aryl halides

A thesis/dissertation
submitted to the Graduate School of UNIST
in partial fulfillment of the
requirements for the degree of
Master of Science

Doyon Kim

June 11, 2019

Approved by



Advisor

Minsang Kwon

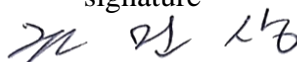
Design of highly efficient organic photocatalysts for visible-light driven reductive dehalogenation of aryl halides

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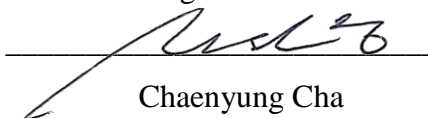
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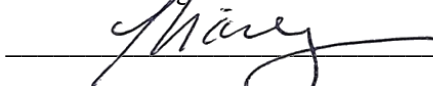
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Abstract

Abstracting halide ions from organohalide compounds and generating free-radical to produce reactive intermediate have proven to be very important and useful step in chemical synthesis and have also found numerous applications in the synthesis procedures. Hence, many scientists have thrived to improve and promote this dehalogenation process to more efficient, simple, and environmentally friendly way. Adoption of photocatalytic way, the conversion of light energy into chemical energy, was the most prominent of all, as it is the inexpensive and sustainable way to induce chemical reactions. It is widely known to utilize inorganic photocatalysts such as iridium or ruthenium complex catalysts with high concentration relative to substrate in dehalogenation. However, their hazards and toxicity were of great concerns, thus many researches were done to make use of organic photocatalysts. Still there have been many problems such as involving UV region for the activation of catalysts, requisites for harsh condition, high catalyst loading or difficulties in reducing chloro- or electron rich bromo aryls. So here in we present purely organic photocatalyst designed to attain sufficient triplet lifetime to achieve visible light mediated single electron transfer process (SET). It successfully demonstrates facile dehalogenation in mild condition with most of the aryl halides, even with the chloro- and electron rich bromo aryls which are reported to be difficult to reduce, and also shows remarkable yield with catalyst loading down to sub-ppm level. In addition, oxygen tolerance feature of the catalyst notes that not only singlet state but also triplet state should be taken a close look at.

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I. Introduction

Utilizing sunlight as the useful energy source for chemical reaction has been the prominent area of research for decades.¹ As the green energy is the popular subject regarding sustainable energy, many researches are being made to harness sunlight as abundant energy source, especially visible light. Amongst many methodologies, photocatalyst, which absorbs light to be activated to excited states, has been actively researched and applied to many areas. Especially applying photoredox chemistry to radical chemistry, which is the most facile way and direct means to access chemical synthesis, is the most actively researched area recently.²

Radical reactions are very powerful way to initiate the chemical transformation. However, the traditional way of generating the radical engaged toxic reagents such as tributyltin hydride, making the reaction process complicated. Hence organo-metallic photocatalysts came to emerge as the substituents to create the radical from activated or unactivated alkyl, alkenyl and aryl halides.² These organo-metallic catalysts are easy to tune their reduction potential by changing the center metal or peripheral ligands. Widely used organo-metallic photocatalysts are Ir or Ru centered catalysts such as *fac*-Ir(ppy)₃, Ru(bpy)₃Cl₂, [Ir{dF(CF₃)ppy}₂(dtbbpy)]PF₆ or Ir(ppy)₂(dtbbpy)PF₆. Among these, *fac*-Ir(ppy)₃ has the highest reduction potential and is efficiently able to undergo radical reductive cleavage of carbon-halide bond.² By breaking carbon-halide bond and generating carbon radical, this radical can go through countless organic reaction processes, representatively the formation of carbon-nitrogen bond or carbon-carbon bond, radical cyclization and also substituting halogen atom to hydrogen atom without interfering other functional groups.³⁻⁵ This paper will specifically focus on our specially designed photocatalyst's ability to reduce aryl halide groups, taking off halide ion and substituting its place with hydrogen: the reaction called dehalogenation.

Recently, dehalogenation via photoredox chemistry has enabled the development of radical transformation of chemical molecules.⁶⁻⁸ This method uses photocatalysts that excites by absorbing the light, making highly reducing or oxidizing excited state which makes it possible to facilitate the redox-based transformation. So, there were many researches done to make this photocatalytic redox dehalogenation process facile, mild, inexpensive, simple and most of all environmentally friendly. However, past works regarding dehalogenation experiments mainly used iridium or ruthenium-based metal catalysts, which are more expensive than pure organic catalysts, and usage of rare earth metal catalyst also raised the problem of purification after the experiment. So, until now many pure organic photoredox catalysts have been made and put into use to abstract the halide ion from various halide substrates, but these organic photocatalysts still have the problems such as requirements for high concentration of catalyst⁹, UV light irradiation^{7, 8}, or harsh reaction condition⁹. Plus, they are mostly only able to reduce activated alkyl, alkenyl, aryl halides or iodide substrates which are easy to reduce compared to bromide, chloride substrates or unactivated aryl halides.^{7, 9} But with employment of our

purely organic photocatalyst 4DP-IPN, which has donor-acceptor twisted structure to intensify charge transfer character, it was possible to reduce aryl halides with electron donating group with very low concentration of catalysts in presence. With adequate excited state oxidation potential (-1.41 V vs. SCE) and ground state oxidation potential ($+1.01\text{ V vs. SCE}$), dehalogenation cycle is able to run stable with only little amount of catalyst, and efficient absorption at visible light range ($\sim 500\text{ nm}$) along with long triplet life time ($\sim 100\text{ }\mu\text{s}$) increase the reaction yield to considerable value.

Along with the latest discovery of oxygen tolerance of organic photocatalyst⁷, we could also observe the tolerance of 4DP-IPN at high catalyst concentration, making the preparation of experiment much simple without having to use the glovebox. But as ppm-level concentration of catalyst doesn't show oxygen tolerance, we thought that amount of catalyst concentration could have effect on the oxygen tolerance because of the reaction rate and tried to unveil the role of singlet and triplet excited state of the catalyst. Hence, we seek to look closely into the unknown photophysical property of photocatalyst and dehalogenation mechanism, providing insight to the future works.

II. Past work review

2.1 Dehalogenation by organometallic photocatalysts

Stephenson et al. (2009)² highlighted the use of sun light as the next generation energy source and tried to utilize it fully to the radical chemistry. This work had presented tris(2,2'-bipyridyl)ruthenium(II) Chloride[Ru(bpy)₃Cl₂] (Fig. 1a) as the main photoredox catalyst to undergo tin-free reductive dehalogenation, and as the potential means to access traditional radical chemistry. The paper shows the simple dehalogenation of complex molecules, abstracting halide ions from the molecule and substituting its place with hydrogen atom, and also argues that this photocatalytic dehalogenation has chemoselectivity by showing that alkyl bromides and chlorides α to electron withdrawing group are reduced better than aryl iodide or bromide.

Stephenson et al. (2012)⁶ tries to improve their work by utilizing other organometallic photocatalyst to generate free radical from unactivated alkyl, alkenyl and aryl iodides with visible light. Here they use *fac*-Ir(ppy)₃ (Fig. 1b) and solves the existing problem of side reaction of metal-halogen exchange and functional group tolerance. They present iridium complex as the substitute of toxic organo-tin and highlights the advantage of metal-based catalyst which is the availability of regulating the redox potential of the catalyst by replacing the ligand or carbon center. The paper shows the reduction of alkyl, alkenyl, aryl iodides owing to the highly negative reduction potential of *fac*-Ir(ppy)₃, and also mentions that even though reduction potential of the substrate is higher than excited state oxidation potential of the catalyst, the substrate can be reduced. One more interesting thing to point out in this paper is it refers that acetonitrile in reaction shows better results after 24 hours reaction than using *N, N'*-dimethylformamide as solution.

Lee et al. (2012)¹⁰ highlights the application of photocatalyst [Ir{dF(CF₃)ppy}₂(dtbbpy)] PF₆ (Fig. 1c) to the unactivated alkyl, alkenyl, aryl halides. This work tried to harness visible light to reductive transformation, mainly demonstrating radical cyclization and dehalogenation of iodide substrates. Research says that replacing conventionally used 20 W CFL with blue LED shows improvement in yield and emphasizes that α carbonyl bromine and chlorine reduces well, just as Stephenson et al. (2009)² mentioned. Also, through labelling experiment, this work showed that hydrogen replacing the halogen atom is abstracted from α -amino place of aminium radical cation of DIPEA.

Barriault et al. (2013)¹¹ points out that ruthenium and iridium complex catalysts have the limit of only being able to reduce highly activated or weak carbon-halogen bonds such as polyhalo-methanes, bromomalonates, electron-deficient benzyl halides, and alkyl/aryl iodides. This work utilizes dimeric gold complex (Fig. 1d) to efficiently generate carbon-centered radical intermediates from unactivated alkyl and aryl bromides in mild condition. They also emphasize the achievement of C-Br bond scission, which couldn't be done with Iridium-based catalysts in Lee's work¹⁰ by metal to ligand charge transfer

(MLCT), and concludes that photoredox application can be possible with not only intramolecular transformation, but also with intermolecular transformation making carbon-carbon bond.

Previously used organometallic photocatalysts

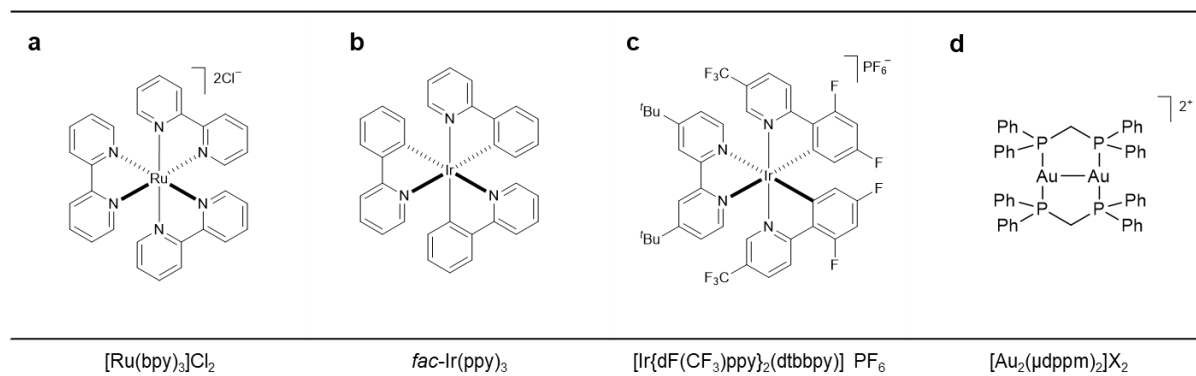


Fig. 1. Organometallic photocatalysts in previous literatures

2.2 Dehalogenation by purely organic photocatalysts

Organic molecules were initially known to have limitation on absorbing the light, and because of the weak spin-orbit coupling compared to heavy metal, organic molecules weren't explored much as catalysts. As efficient photocatalysts should be excited by light and its excited electron must retain the excited state as long as possible, metal-based catalyst's 100% intersystem crossing yield from singlet to triplet owing to its strong spin orbit coupling and quite long triplet lifetime were considered good qualities as photocatalysts and had been studied on as catalyst for photoredox dehalogenation. However, in 2012, Adachi group had synthesized highly efficient organic light-emitting diodes from delayed fluorescence, by combining spatially separated donor and acceptor moieties.¹² Orthogonally placing the donor and acceptor moieties by steric hindrance results in localizing the highest occupied molecule orbital and the lowest unoccupied molecular orbital on the donor and acceptor moieties respectively, leading to small singlet and triplet energy difference, ΔE_{ST} . Hence with their organic molecule 4Cz-IPN (Fig. 2a), intersystem crossing of electron from singlet state to triplet state is easily done by small energy gap, with longer triplet lifetime compared to organo-metallic photocatalysts. Inspired by this work, many researches were done synthesizing similarly structured organic molecules and applying the molecules as catalysts to photoredox chemistry.^{13, 14}

One more limitation that was known for visible light photocatalysis was the energetic limitation. König et al. (2014)⁹ presents perylene diimides (PDI) (Fig. 2b) as the solution for this energetic limitation, molecule donating electron by consecutive visible light-induced electron transfer process. PDI gets excited by visible light and gets reduced by amine, obtaining stable radical anion state in inert environment. Then it gets excited again to excited radical anion state, then donates the electron to the substrate. By being consecutively excited, PDI can achieve the reducing power that reaches or exceeds the reduction potential of substituted aryl chlorides. The paper shows successful carbon-carbon bond formation from various substituted aryl halides using amines and visible light with excess amount of trapping agent. König et al. (2018)¹⁵ adapted the same strategy again in dehalogenation, this time presenting 1,8-dihydroxyanthraquinone (Aq-OH) (Fig. 2e) as photocatalyst. Its excited state of radical anion acts as powerful reductants, so authors employ Aq-OH as photoredox catalyst for aryl halide substrates. But remaining limitation of this work and their previous works are the too high concentration of catalyst (10 mol% relative to the substrates) and limits of the substrate scope, being unable to reduce substrates having extremely high reduction potential such as 4-bromoanisole.

Hawker and Alaniz et al. (2015)⁷ had used 10-phenylphenothiazine (PTH) (Fig. 2c), which they had used as a metal-free catalyst for photomediated atom transfer radical polymerization¹⁶, but this time as catalyst for dehalogenation. PTH acts as a photoreductant in a similar manner to *fac*-Ir(ppy)₃ with a reduction potential ($E_{1/2}^* = -2.1$ V vs. SCE) which is significantly higher than that of *fac*-Ir(ppy)₃ ($E_{1/2}^* = -1.7$ V vs. SCE). This paper highlights PTH's superiority compared to PDI and shows successful

dehalogenation of various aryl halides with 380nm light, even with aryl chlorides. Moreover, the open-air experiment with high dehalogenation yield in this paper emphasized that not only triplet but singlet could also participate in the photoredox process of dehalogenation, seeing that oxygen quenches the triplet. Also, Hawker and Alaniz et al. (2016) had transformed their PTH catalyst to tris-acetyl-PTH (Fig. 2d) by adding acetyl group on benzene and phenothiazine respectively to adjust the potential of the catalyst. Tris-acetyl-PTH displayed low reduction potential ($E_{1/2}^* = -1.5$ V vs. SCE) compared to PTH, hence showing inferior result to PTH when reducing 3-bromopyridine and methyl 4-chlorobenzene. When PTH could reduce all aryl halides even aryl chlorides, tris-acetyl-PTH was only able to reduce aryl iodides. Hence, this work showed that organic photocatalyst could show chemoselectivity by adjusting the donor and acceptor moieties by little, reducing the desired halogen only when there are more than two kinds of halogen atoms attached to aryl substrates.

Previously used purely organic photocatalysts

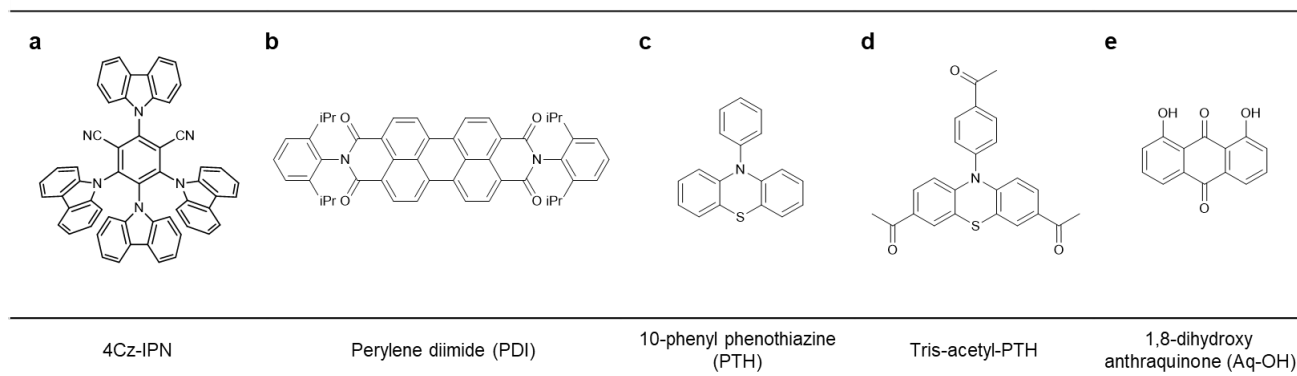


Fig. 2. Organic photocatalysts in previous literatures

III. Catalyst design and dehalogenation mechanism proposal

3.1. Organic photoredox catalyst design logic

When designing organic photoredox catalyst to run the reaction cycle nicely, there are several factors to consider. Catalyst's singlet and triplet state's energy gap, ΔE_{ST} should be small enough for the excited electron of the singlet state to go through intersystem crossing to triplet state¹⁷, and the triplet lifetime should be sufficiently long enough for the catalyst to meet with the substrate within the lifetime of triplet electron. We first investigated our reference catalyst 4Cz-IPN synthesized by Adachi group to spread out to similar analogues.¹⁴ Considerably small $\Delta E_{ST} \leq 0.2$ eV was attainable by intramolecular charge transfer within systems containing spatially separated donor and acceptor moieties. Carbazole units are quite distorted from dicyanobenzene group due to the steric hindrance, localizing HOMO and LUMO to donor and acceptor moieties respectively, leading to a small ΔE_{ST} . Also, radiative decay rate should be over 10^6 s⁻¹ to overcome non-radiative pathway. But these two factors conflict with each other so there must exist good balance between HOMO and LUMO. To enhance the photoluminescence efficiency of the catalyst, non-radiative decay should not exist, so S_0 (ground state) and S_1 (singlet state) geometry should be constrained to suppress non-radiative decay. However, if the orbital overlap is limited, then there is virtually no emission, so it was previously known that very small ΔE_{ST} and high photoluminescence was hard to obtain simultaneously. But Adachi group had made it possible by introducing cyanobenzene derivatives as acceptor group and carbazole derivatives as donor group of the thermally activated delayed fluorescence organic molecule.¹² Hence, we also tried to synthesize suitable organic photocatalyst by combining appropriate donor and acceptor moieties.

According to the organic photocatalyst design logic of Kwon et al. (2018)¹⁸, strong charge transfer character of S_1 is the key factor for controlling the light absorption and redox potential of ground and excited state of the catalyst. By changing donor and acceptor group of the catalyst, it is possible to control HOMO-LUMO energy gap. Replacing the donor moiety changes the ground state oxidation potential and excited state reduction potential of the catalyst, and replacing the acceptor moiety changes the ground state reduction potential and excited state oxidation potential of the catalyst.

We assumed that our dehalogenation experiment goes through oxidative quenching cycle referring to our reference paper², so it was important to consider catalyst's excited state oxidation potential value (E_{ox}^*) for it to give electron to substrate from its excited state, and ground state oxidation potential (E_{ox}^0) for the catalyst to abstract electron from the electron donor and return to its original state. Considering oxidative quenching, stability of radical cation was also of issue.¹⁹ Also, retaining the twisted donor-acceptor structure for the charge transfer character for the efficient generation of long-lived triplet was also of importance and was set to basic. Changing the donor moiety to strong one such as diphenyl

amine or dimethoxy diphenyl amine increases the visible light absorption and stabilizes the radical cation. Changing the acceptor moiety to weaker one elevates the E_{ox}^* value to make the catalyst highly reducing, hence being able to reduce aryl halide substrates with high reduction potential.

Following this logic, we synthesized 4DP-IPN (Fig. 3a) and 4DMDP-IPN (Fig. 3b) - changing the carbazoles of 4Cz-IPN to diphenyl amines and dimethoxy diphenyl amines respectively— where the donor is strong in dimethoxy diphenyl amine, diphenyl amine, carbazole order. Also, we synthesized 4DP-BN (Fig. 3c), by setting the acceptor as benzonitrile, which is a weaker donor than isophthalonitrile (IPN) and substituting 2,3,5,6 sites with diphenyl amines. Each of these three catalysts displayed different characteristics (Fig. 4).

Unfortunately, even though 4DP-BN has high excited oxidation potential to reduce the substrates, it doesn't have good solubility with the solvent acetonitrile (MeCN) that we use for the experiment, so we were only able to use it with *N,N'*-dimethylformamide (DMF) in some additional experiment. 4DMDP-IPN has high enough excited oxidation potential and nice solubility but didn't really show good results from dehalogenation with our representative substrates. We concluded that because it has the low ground state oxidation potential due to strong donor, its ability to close the catalyst cycle by abstracting the electron in the form of radical cation is poor. From here we noticed that ground state oxidation potential is also an important factor as the catalyst for dehalogenation. 4DP-IPN has proper E_{ox}^* (~ -1.41 V vs. SCE) and E_{ox}^0 (~ 1.01 V vs. SCE) to open and close the dehalogenation cycle with most of the substrates, along with excellent solubility and as well as stable radical cation form, so we chose 4DP-IPN as our representative organic photoredox catalyst (Fig. 5).

Newly synthesized organic photocatalysts

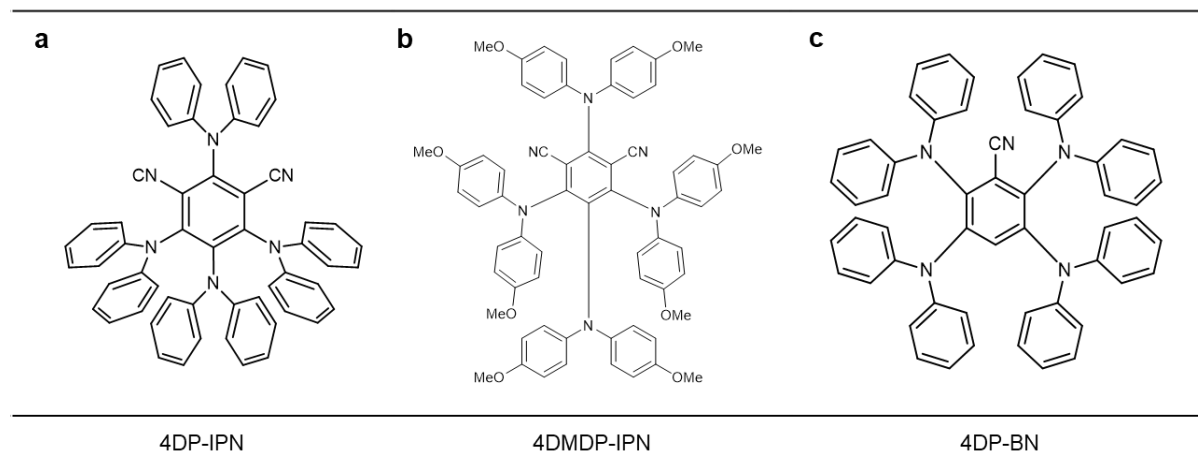


Fig. 3. New organic photocatalysts synthesized via catalyst design logic

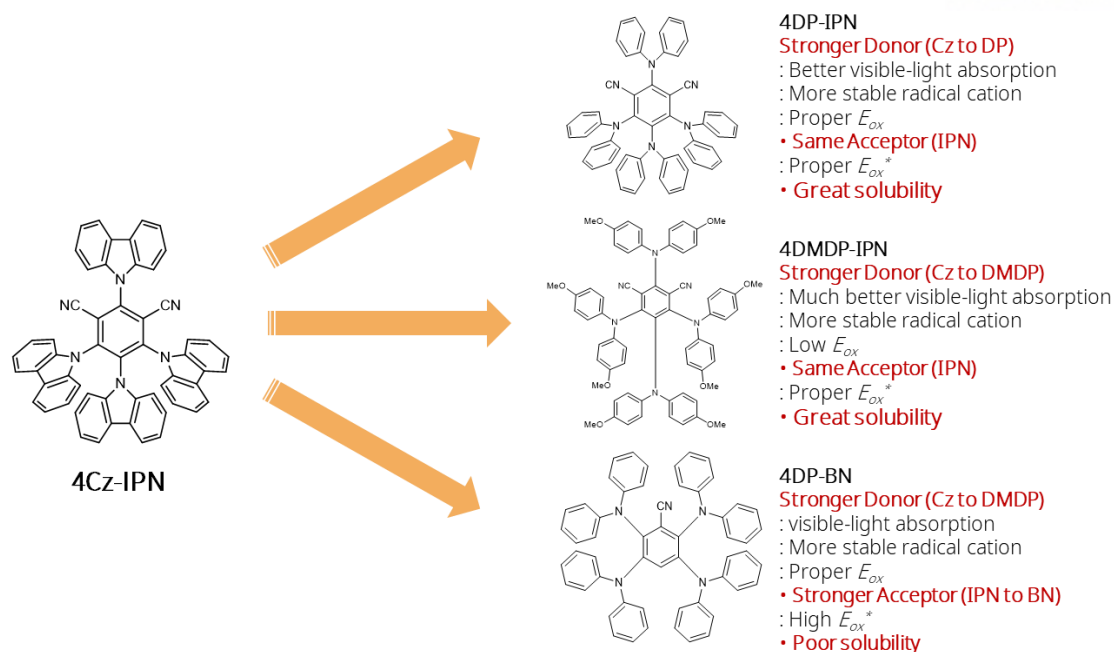


Fig. 4. Newly designed photocatalyst's characteristics

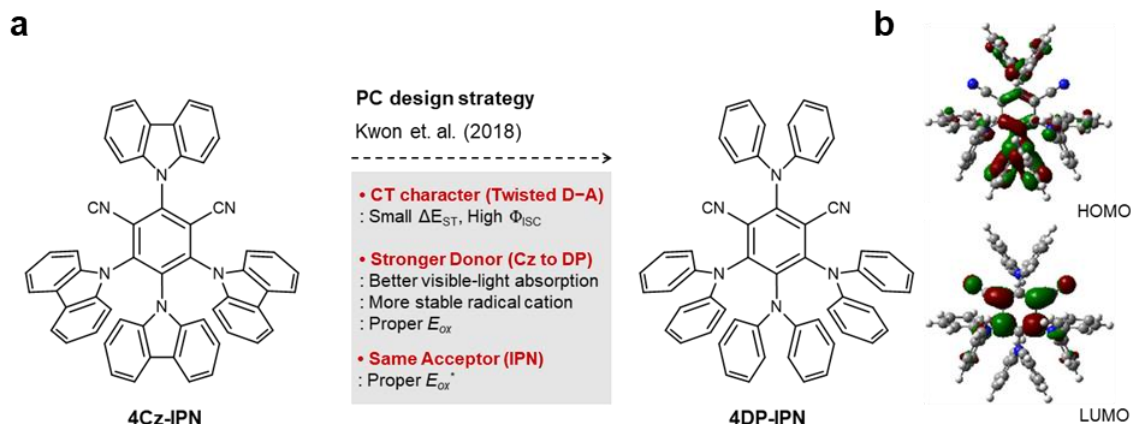


Fig. 5. (a) Design of 4DP-IPN from 4Cz-IPN (b) Calculated HOMO and LUMO topologies of 4DP-IPN

3.2. Mechanism proposal

Stephenson et al. (2012)² had proposed that dehalogenation utilizing *fac*-Ir(ppy)₃ as photoredox catalyst goes through oxidative quenching cycle, with the evidence that alkyl iodide substrate showing virtually no yield without amine as electron donor or hydrogen donor in the reaction. There is no electron donor to effect catalyst turnover and the propagation chains are short lived. Hence, they proposed that the mechanism of the reaction involves the oxidative quenching of *fac*-Ir(ppy)₃* by the alkyl, alkenyl and aryl halide. There are also many other works stating that dehalogenation process adapting photoredox catalyst undergoes the oxidative quenching cycle.

Therefore, we also concluded that our dehalogenation process utilizing 4DP-IPN as catalyst also mainly goes through oxidative quenching cycle.^{5, 7, 9}

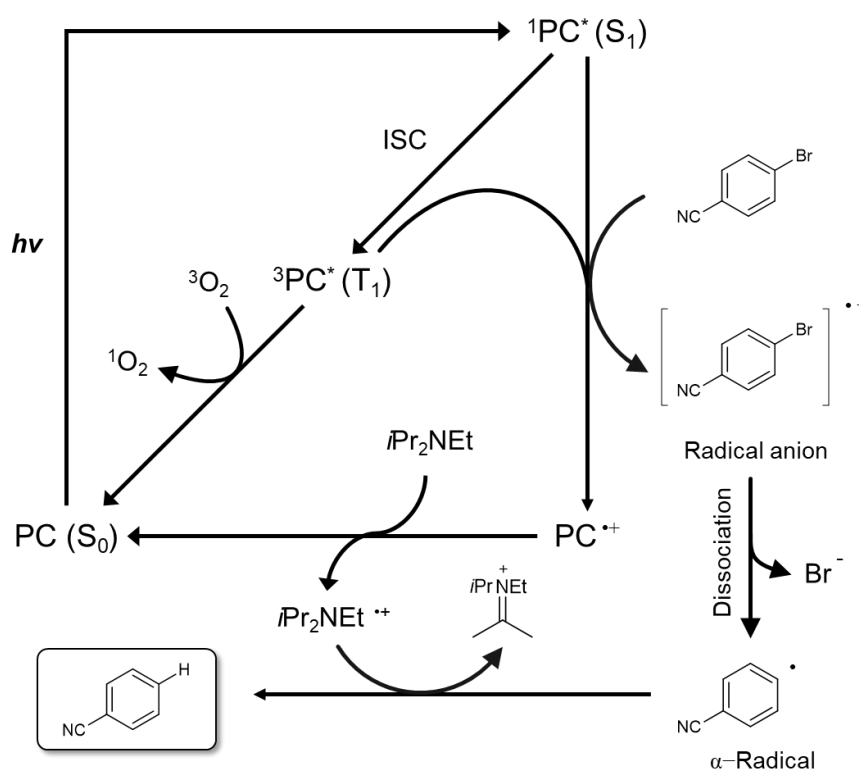


Fig. 6. Proposed mechanism of dehalogenation of aryl halides

First, PC (photocatalyst) gets excited by the light source from ground state (S_0) to the singlet state (S_1) and some excited electrons from S_1 shifts to triplet state (T_1) by intersystem crossing. Then electrons from singlet or triplet state of PC gets transferred to aryl halide substrate, producing radical anion substrate, and thereby catalyst being radical cation. Radical cation form of PC abstracts electron from sacrificial reagent diisopropylethylamine (DIPEA) and returns to its original form, again getting excited

by light and runs the catalyst cycle again. Triplet state (T_1) can return to ground state by oxygen quenching. From radical anion complex of substrate, halogen gets dissociated and becomes α -radical. Then finally, bromine dissociated α -radical abstracts the hydrogen from aminium radical cation of DIPEA, yielding the dehalogenation product of aryl halide substrate. It was determined in other literatures with labelling experiment that α -radical substrates don't abstract hydrogen from MeCN solvent, and only abstracts from sacrificial amine.^{7, 10}

IV. Experiment results and discussion

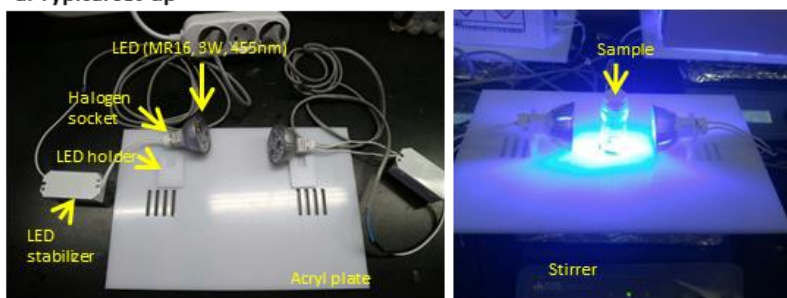
4.1. Optimization of general reaction condition

On starting dehalogenation experiment, it was important to find the optimized reaction condition to get the best result. We started by following the reaction condition of the previous literature.⁷ General reaction condition is fixed to substrate 0.1 M (1 equiv.), internal standard for NMR and gas chromatography measurement 0.2 M, catalyst concentration 5 ~ 0.001 mol%, DIPEA as sacrificial electron and hydrogen donor (10 equiv.), with MeCN solvent 1 mL.

Organic photocatalyst 4DP-IPN is used as main catalyst in the experiment. First, 4DP-IPN (4.2 mg, 5 mol% amount) is put into MeCN 1 mL in 20 mL vial. Then add substrate (0.1M) and DIPEA (0.174 mL, 10 equiv.) along with 1,3,5- trimethoxybenzene (0.2M, 33.6mg) as internal standard. The reaction mixture in vial is then purged with argon for 30 minutes. Next, the reaction vial is put into the LED setup (Fig. 7) and is run until it reaches the highest yield. Light source is 6W 455 nm blue LED and dehalogenation reaction was carried out in either argon (inert) or air environment.

Conversion and yield were calculated using gas chromatography (GC) or NMR with 1,3,5-trimethoxybenzene or 1,2,4,5-tetramethyl benzene as internal standard.

a. Typical set-up



b. 6W LED set-up



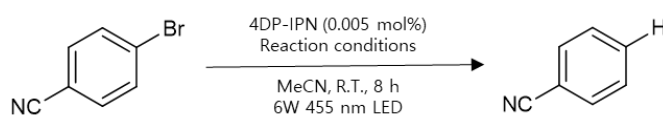
c. 12W LED set-up



Fig. 7. LED setup (a) typical set-up (b) 6W LED set-up (c) 12W LED set-up

Previous literatures had used various sacrificial agents as electron and hydrogen donors such as triethylamine, tributylamine, formic acid, DIPEA and their combination. We also wanted to optimize our reaction by changing the conditions. After trying various combinations, we concluded that only using DIPEA in excess amount (10 equiv.) yields the best result (Table 1, entry 11).

Table 1. Optimization of use of electron and hydrogen donors

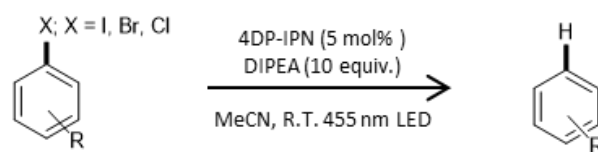
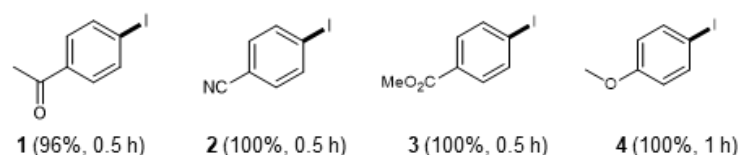
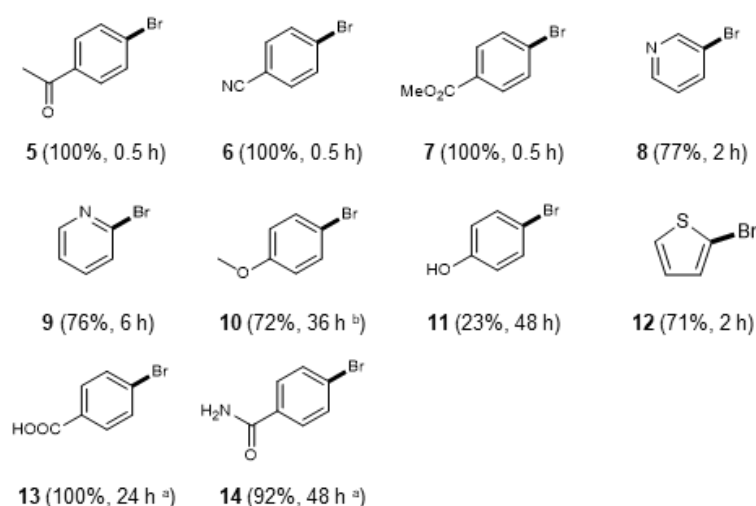
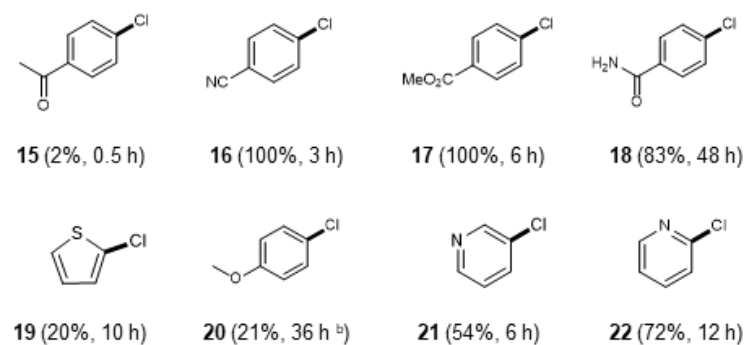


Entry	Reaction conditions	Yield (%)
1	TEA (5.0 equiv.)	0
2	TEA (5.0 equiv.), Formic acid (5.0 equiv.)	1.02
3	TEA (10.0 equiv.)	4.70
4	TEA (10.0 equiv.), Formic acid (10.0 equiv.)	59.44
5	TBA (5.0 equiv.)	2.42
6	TBA (5.0 equiv.), Formic acid (5.0 equiv.)	3.81
7	TBA (10.0 equiv.)	73.08
8	TBA (10.0 equiv.), Formic acid (10.0 equiv.)	92.47
9	DIPEA (5.0 equiv.)	74.84
10	DIPEA (5.0 equiv.), Formic acid (5.0 equiv.)	90.51
11	DIPEA (10.0 equiv.)	100

4.2. Expanding dehalogenation substrate scope

Previous works which demonstrated dehalogenation with photoredox catalysts had limits on its substrate scope such as not being able to reduce aryl halides with electron donating group attached on it.¹⁵ So here in we did the experiment to prove the performance of our organic photoredox catalyst 4DP-IPN, with various aryl halide substrates even with the ones that were not explored deeply before, in very mild reaction condition.

Figure 8 shows the dehalogenation results with various aryl halide substrates. Aryl iodide substrates which are known to be much easier to reduce compared to aryl bromides and chlorides were reduced well as expected. All the aryl iodide substrates showed high yield up to 100%, in very short time range (Fig. 8, entries 1-4). Even 4-iodoanisole (Fig 8, entry 4) which has electron donating group at *para*- site was reduced completely after 1 hour. Several aryl bromides were also reduced successfully within 30 minutes (Fig. 8, entries 5-7). Heterocyclic molecules (Fig. 8, entries 8, 9, 11) also showed high yield. Most interesting result is high dehalogenation yield with 4-bromoanisole (Fig 8, entry 10), which was previously reported as a hard molecule to reduce, only showing meaningless yield with other photoredox catalysts. Encouraged by aryl bromide substrate results, we tried aryl chloride substrates also, which are harder to abstract the halogen from than aryl bromide or aryl iodide. Ones with electron withdrawing group attached on it showed decent result (Fig. 8, entries 16-18). 4-Chloroacetophenone (Fig. 8, entry 15) showed 100% conversion on GC and NMR, but there was no product to be found. This phenomenon was also reported in other literature.¹⁹ And as expected, 4-chloroanisole (Fig. 8, entry 20) showed low yield even after quite long reaction time, and we concluded that this is due to very high reduction potential of the molecule. Availability of the catalyst to reduce the substrate depends on the substrate's reduction potential. If the reduction potential is high, then it is difficult for the catalyst to reduce the substrate to α -radical.²⁰

**Aryl iodide****Aryl bromide****Aryl chloride**

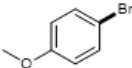
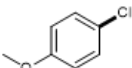
Reaction conditions: Substrate (1 equiv.), 4DP-IPN (5 mol%), DIPEA (10 equiv.), acetonitrile (0.1 M of substrate) at R.T. with irradiation by two 455 nm LEDs (5 mW/cm²). GC yield determined using 1,3,5-trimethoxybenzene or 1,2,4,5-tetramethylbenzene as an internal standard. ^a Reaction was performed in DMF. ^b Reaction was performed with four 455 nm LEDs (10 mW/cm²).

Fig 8. Photo-reductive dehalogenation of aryl halides

To see 4DP-IPN's performance with dehalogenation better, we used other known catalysts 4Cz-IPN and *fac*-Ir(ppy)₃ in same dehalogenation reaction and compared the result (Table 2). Yields were taken and recorded every 12 hours (Fig. 9). For 4-bromoanisole, 4DP-IPN showed superior results to other catalysts, yield over 70%, when other catalysts only showed yield under 30%. Experiment with 4-chloroanisole showed same tendency, still 4DP-IPN demonstrating highest yield whereas *fac*-Ir(ppy)₃ showed no yield.

In conclusion, by utilizing 4DP-IPN, we could successfully reduce various aryl halide substrates and expand the substrate scope, including the ones that were not reported before.

Table 2. Comparison of reduction capabilities of *fac*-Ir(ppy)₃, 4Cz-IPN with 4DP-IPN for the reduction of 4-bromo- and chloroanisole.

Ph-X		Photoredox catalyst (5 mol%) DIPEA (10 equiv.) MeCN, R.T. 455 nm LED, Ar		Ph-H
Substrate	Time	Photocatalyst	Yield	
	36 h	4DP-IPN	72%	
		4Cz-IPN	26%	
		<i>fac</i> -Ir(ppy) ₃ ^a	17%	
	24 h	4DP-IPN	21%	
		4Cz-IPN	11%	
		<i>fac</i> -Ir(ppy) ₃ ^a	0%	

Reaction conditions: 4-Bromo or Chloroanisole (1 equiv.), PC (5 mol%), DIPEA (10 equiv.), acetonitrile (0.1 M of substrate) at R.T. with irradiation by four LEDs. GC yield determined using 1,3,5-trimethoxybenzene as an internal standard. ^a Reaction was performed in DMF.

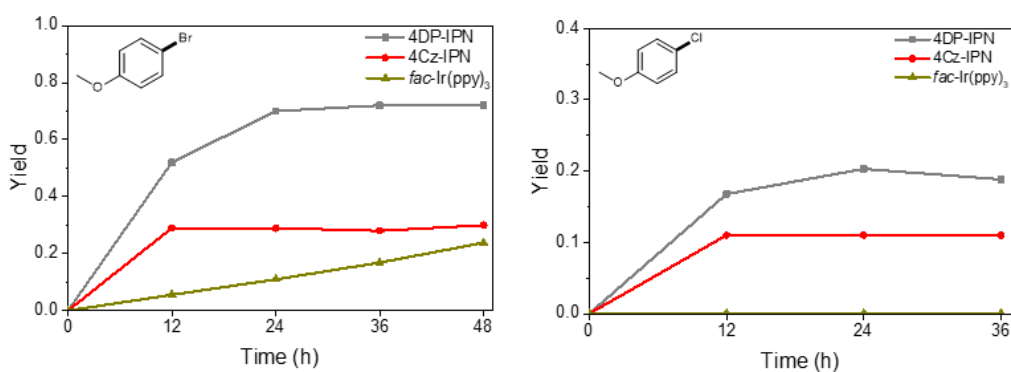
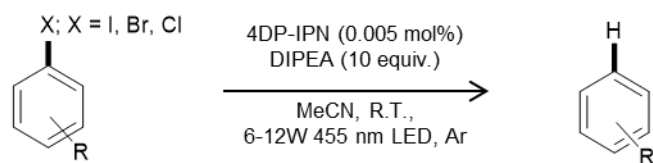


Fig. 9. Photo-reduction of 4-bromo- and chloroanisole yield value taken every 12 hours

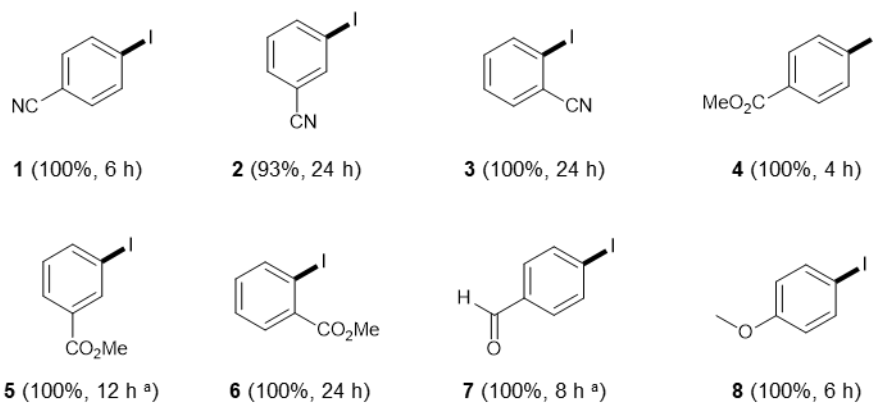
4.3. Lowering catalyst loading to sub-ppm level

Dehalogenation reaction went successfully with 5 mol% of catalyst amount relative to the substrate, only taking below 1 hour for aryl iodide substrates. Even aryl bromides with electron withdrawing group as the functional group were reduced within quite short time range. Compared to the dehalogenation results of other literatures using same amount of catalyst^{7,9}, our reaction time reaching the maximum yield was considerably short. It was highly probable that even if we lower the catalyst concentration, the reaction will still go fine. So lowered the catalyst concentration from 5 mol% to 0.005 mol%, relative to the substrate amount, with other reaction conditions staying the same. (Fig. 10)

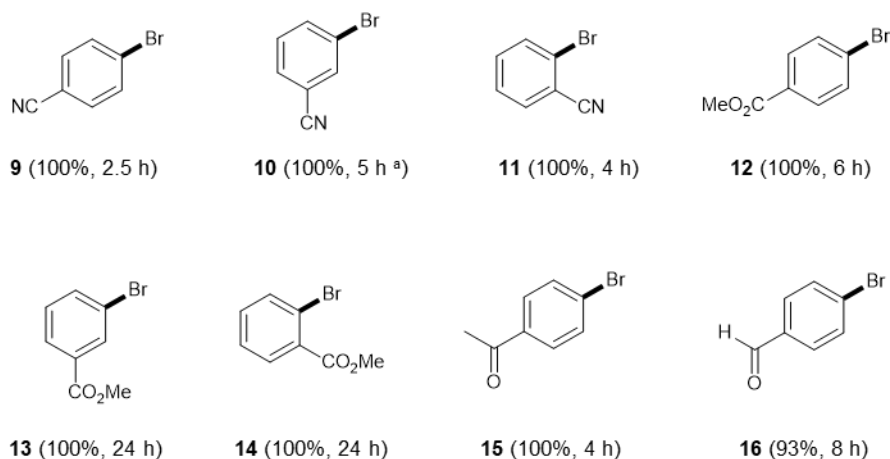
Aryl iodides with functional groups attached on *para*- site were reduced with 100 % yield within short time range (~ 6 hours) (Fig. 10, entries 1, 4, 8). Although other substrates need more time, they were fully reduced within 24 hours. Even aryl bromide substrates were reduced successfully with 0.005 mol% catalyst concentration (Fig. 10, entries 9-16). Reaction with strongly activated aryl chlorides also achieved high yield, though it needed higher catalyst concentration (0.05 mol%) and stronger light (12 W) (Fig. 10, entries 17-18).



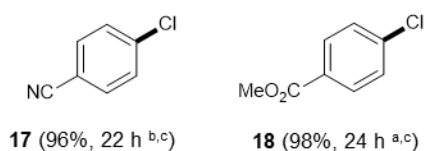
Aryl iodide



Aryl bromide



Aryl chloride



Reaction conditions: Substrate (1 equiv.), 4DP-IPN (0.005 ~ 0.5 mol%), DIPEA (10 equiv.), acetonitrile (0.1 M of substrate) at R.T. with irradiation by two LEDs. GC yield determined using 1,3,5-trimethoxybenzene as an internal standard. Reaction was performed with ^a0.01 mol%, ^b0.05 mol% and ^cfour LEDs.

Fig. 10. Photo-reduction of aryl halides with ppm-level amount of photocatalyst

Next, we did the comparison experiment with conventional photoredox catalyst *fac*-Ir(ppy)₃, lowering *fac*-Ir(ppy)₃ concentration from 0.05 mol% to 0.001 mol%, using 4-bromobenzonitrile as substrate with other conditions staying the same (Fig. 11). Whereas 4DP-IPN showed 100 % yield down to 0.005 mol% catalyst concentration, *fac*-Ir(ppy)₃ showed poor yield from 0.05 mol%. We thought that the reason 4DP-IPN shows better yield compared to *fac*-Ir(ppy)₃ is the very long lifetime of 4DP-IPN (70~100μs) compared to *fac*-Ir(ppy)₃ (1μs). Although the possibility of catalyst meeting the substrate becomes very small when lowering the amount of catalyst, and though the electron transfer rate is slow, triplet lifetime is sufficiently long enough to react and donate the electron to the substrates (Fig. 12). So it is possible to dehalogenase aryl iodides, bromides and chlorides even with very little amount of organic photoredox catalyst.

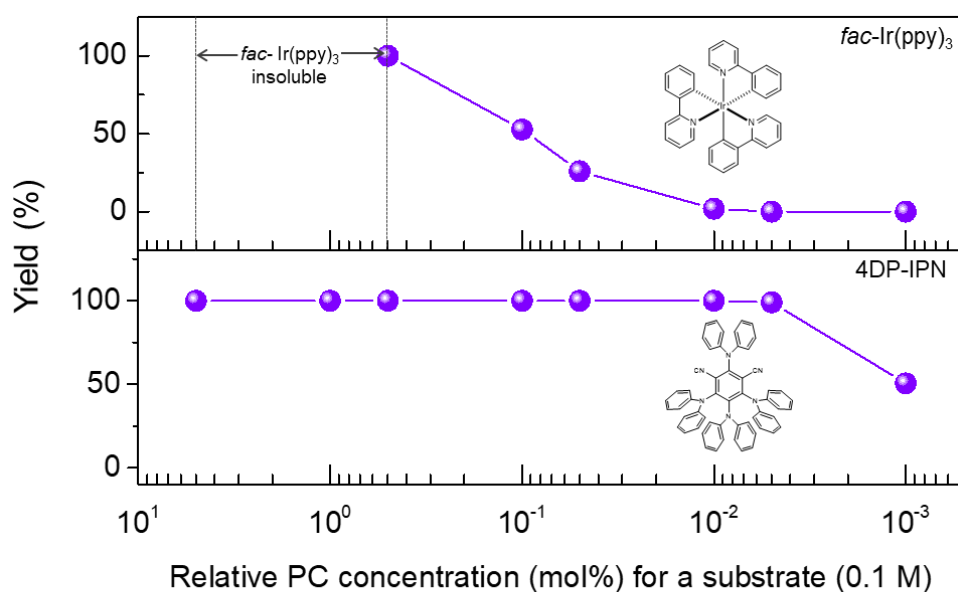


Figure. Plots of dehalogenated yield depended on *fac*-Ir(ppy)₃ and 4DP-IPN concentrations. Reaction was monitored until 8 hours. Yield was determined by GC using 1,3,5-trimethoxybenzene as an internal standard. Conditions: 4-Bromobenzonitrile (1 equiv.), PC (5 ~ 0.001 mol%), DIPEA (10 equiv.), acetonitrile (0.1 M of substrate) at R.T. with irradiation by two LEDs.

Fig. 11. Comparison of reduction capabilities of *fac*-Ir(ppy)₃ with 4DP-IPN for the reduction of 4-bromobenzonitrile with lowering catalyst concentration

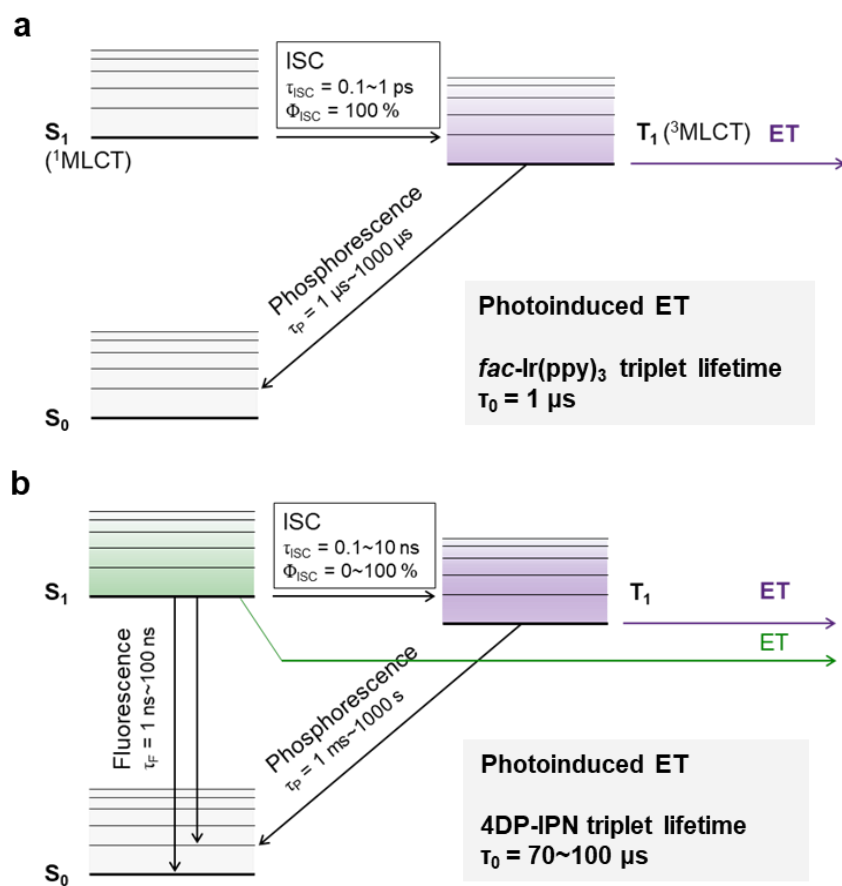


Fig. 12. Energy diagram of (a) *fac*-Ir(ppy)₃ (b) 4DP-IPN and their electron transfer pathways

4.4. Oxygen tolerance of organic photoredox catalyst

In the previous literature by Alaniz et al. (2015)⁷, it had mentioned 10-phenyl phenothiazine's oxygen tolerance in dehalogenation reaction. The open to air reaction with iodobenzene as substrate produced 57 % yield within 2 hours, giving the benzene as the reaction product. As the oxygen in air quenches the triplet, it emphasized that singlet state's role in transferring electron to the substrate. But most of the literatures insists that triplet state play substantial role in electron transfer, and there are still controversies going on.²¹ Hence, we did the experiment to see if there is also oxygen tolerance with our catalyst, 4DP-IPN.

Experiment condition was same with lowering catalyst loading experiment, from 5 mol% to 0.001 mol% relative to the substrate amount. But this time we didn't do the argon degassing (30 minutes) and prepared the reaction vial outside the glove box. Surprisingly, 4DP-IPN showed oxygen tolerance down to 0.05 mol% showing 100 % yield, even with air in presence (Fig. 13). As oxygen quenches the triplet of the catalyst, we thought that with the presence of oxygen, catalyst's singlet state transfers the electron to the substrate. Based on the result of the oxygen tolerance experiment, we concluded that with high catalyst concentration, singlet plays the main role in transferring the electron, and with low catalyst concentration, triplet state.

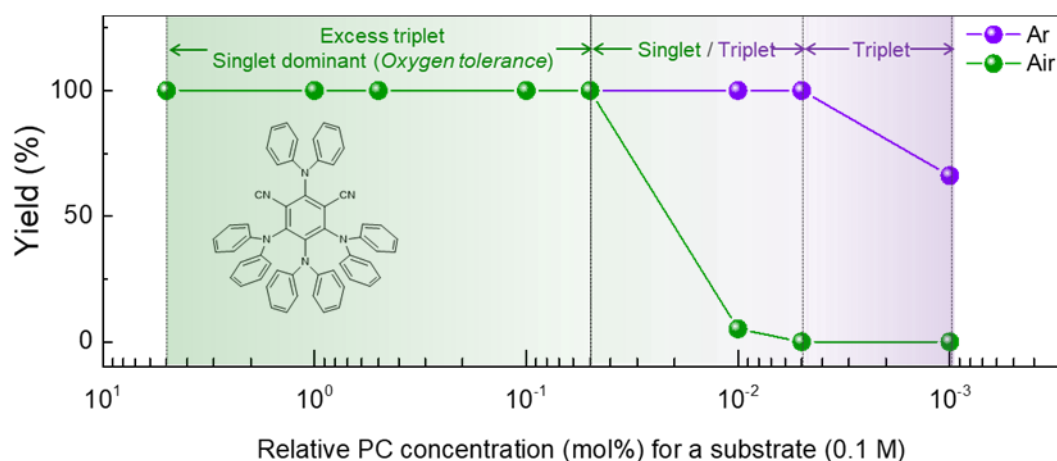


Figure. Plots of dehalogenated yield depended on 4DP-IPN concentration. Reaction was monitored until 8 hours. Yield was determined by GC using 1,3,5-trimethoxybenzene as an internal standard. Conditions: 4-Bromobenzonitrile (1 equiv.) 4DP-IPN (5 ~ 0.001 mol%), DIPEA (10 equiv.), acetonitrile (0.1 M of substrate) at R.T. with irradiation by two LEDs.

Fig. 13. Oxygen tolerance experiment result with 4DP-IPN

Next, we did the comparison experiment using 4Cz-IPN and *fac*-Ir(ppy)₃ (Fig. 14). Organic photoredox catalyst 4Cz-IPN showed similar nature to 4DP-IPN, showing notable yield with high concentration of catalyst, and almost no yield under very low concentration with presence of air. On the other hand, organometallic photoredox catalyst *fac*-Ir(ppy)₃ showed almost no yield with presence of air, which is reasonable as all *fac*-Ir(ppy)₃'s triplets are quenched by oxygen.

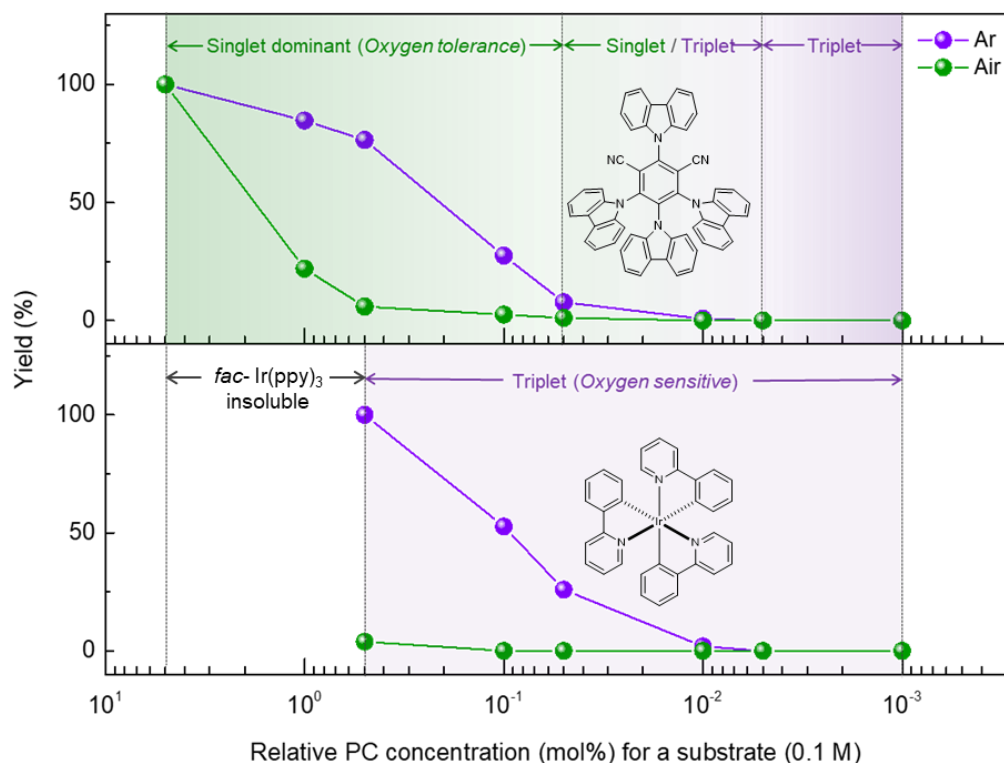


Figure. Plots of dehalogenated yield depended on Ir(ppy)₃ and 4Cz-IPN concentrations. Reaction was monitored until 8 hours and 16 hours respectively. Yield was determined by GC using 1,3,5-trimethoxybenzene as an internal standard. Conditions: 4-Bromobenzonitrile (1 equiv.) PC (5 ~ 0.001 mol%), DIPEA (10 equiv.), acetonitrile (0.1 M of substrate) at R.T. with irradiation by two LEDs.

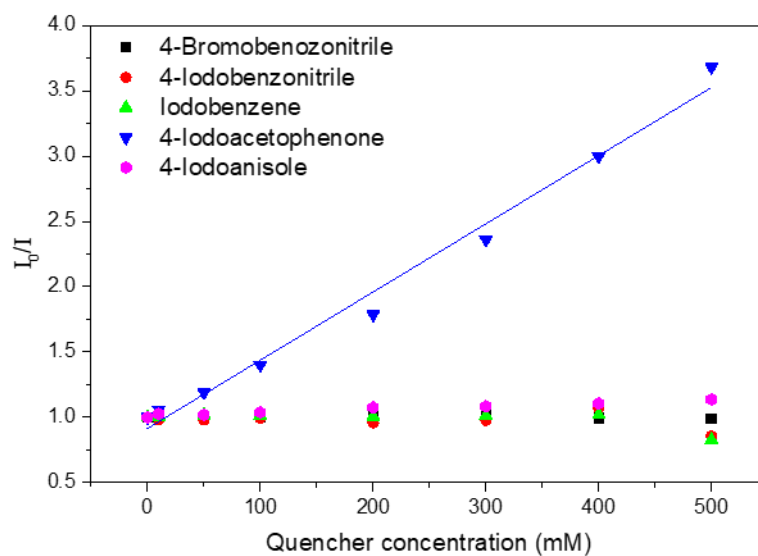
Fig. 14. Oxygen tolerance experiment result with 4Cz-IPN and *fac*-Ir(ppy)₃

To prove that singlet plays the role in electron transfer, we sought to see the singlet quenching with transient photoluminescence.²² With fixed amount of catalyst, we varied the substrate (4-bromobenzonitrile) concentration from 0 M to 1 M, but there was no singlet quenching shown in nano second scale. So, we assumed that the reason that singlet quenching is not shown because of the potential problem, as 4DP-IPN's singlet excited oxidation potential ($E_{ox}^*(S_1) = -1.58 \text{ V vs. SCE}$) is lower than the reduction potential of 4-bromobenzonitrile ($E_{red}^0 = -1.78 \text{ V vs. SCE}$). Based on this hypothesis, we investigated the reduction potential of highly activated aryl iodide substrate's reduction potentials (Table 3) and did the steady state quenching PL experiment with these substrates.

Table 3. 4DP-IPN's excited state oxidation potentials and substrates' ground state reduction potential measured with cyclovoltammetry

4DP-IPN	$E_{ox}^*(S_1) = -1.58 \text{ V (vs. SCE)}$ $E_{ox}^*(T_1) = -1.41 \text{ V (vs. SCE)}$ $(E_{ox}^* = E_{ox}^0 + E_{00})$
Substrate	$E_{red}^0, \text{ starting (vs. SCE)}$
4-Iodoacetophenone	-1.50 V
4-Iodobenzonitrile	-1.70 V
Iodobenzene	-1.89 V
4-Iodoanisole	-1.88 V
4-Bromobenzonitrile	-1.78 V

Among these substrates, only 4-iodoacetophenone which has the lowest ground state reduction potential shows the tendency of decreasing of PL intensity (Fig. 15). When calculating the quenching constant, it shows $10^8 \text{ s}^{-1}\text{M}^{-1}$ scale, which can be competent with fluorescence decay or intersystem crossing rate according to the Jablonski diagram of 4DP-IPN (Fig. 16). In conclusion, 4DP-IPN does show the oxygen tolerance nature in presence of air, but the reason why the substrates with high reduction potential such as 4-bromobenzonitrile don't show the singlet quenching could be due to the high encounter possibility of substrate and the catalyst at the high concentration of catalyst in reaction, plus other factors could have effects in the mechanism. Also, PL quenching experiment cannot display exactly same reaction condition to our real experiment, so there could be deviation of results. We are still exploring deep into more detailed photophysical properties of 4DP-IPN and the mechanism of dehalogenation.



Quenching constant $k_q = 1.7 \times 10^8 \text{ s}^{-1}\text{M}^{-1}$

Fig. 15. Stern-Volmer plot of steady-state PL quenching of substrates with 4DP-IPN

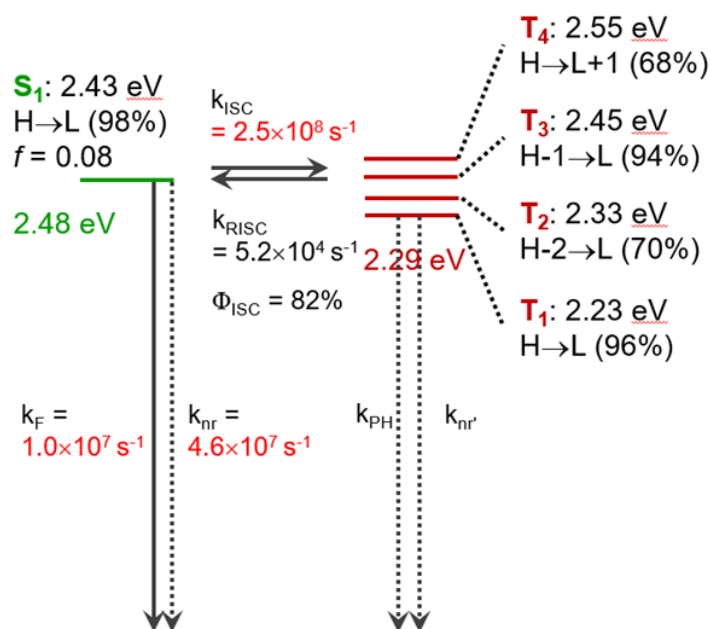


Fig. 16. Jablonski diagram of 4DP-IPN

V. Conclusion

In summary, we have synthesized the new organic photoredox catalyst (OPC) based on the design strategy that can undergo dehalogenation reaction with very mild condition. Broadening the substrate scope including the ones that were thought to be hard to reduce with previously reported OPC and minimizing the catalyst concentration level and still retaining high yield within short time were also done successfully. Finally, it is worth emphasizing the oxygen tolerance of our OPC, demonstrating the high dehalogenation yield with even oxygen in presence. Further studies on the photophysical properties of PC are needed, but still we envision our PC to be applied to radical chemistry reaction in near future.

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